

REMARKS

The foregoing amendment is submitted to make minor changes to the specification to place the same in better form under U.S. practice and to respond to particular objections set forth in the Office Action. In particular, Applicants have provided a new title to the invention which is more descriptive of the invention taking into consideration the amendment to claims discussed below. Proper headings have been provided for the specification including a section entitled "Related Application" and a brief description of the sole drawing discussed on page 8 of the specification.

5 No new matter has been added to the specification and entry to the amendment to the specification is deemed proper and is respectfully requested.

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Applicants have provided a new set of claims (new claims 34-62) focusing on a gelatin composition which comprises 83 to 93% by weight of fish gelatin, 7 to 17% by weight of water and 0.01 to 10% by weight of a hydrocolloid setting system containing at least one of the materials specified in claim 34. Reference to fish gelatin can be found throughout the specification such as, for example, on page 2, lines 26-29. Support for the amount of fish gelatin, water and the hydrocolloid setting system is found on page 5, lines 17-22 and original claim 6. The specific 15 components of the hydrocolloid setting system as set forth in new claim 34 is found on page 4, lines 8-12. The type and amount of the sequestering agents as described in new claims 35, 39 and 40 are found on page 5, lines 4-12. Further details of the hydrocolloid setting system as covered by claims 36, 41-45 are set forth on page 4 beginning at line 5.

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The remaining new claims added by the present amendment find correspondence in the original claims and throughout the specification as filed. No new matter has been added to the application by the presentation of new claims 34-5 62 and entry thereof is deemed proper and is respectfully requested.

Referring to the Office Action, as previously indicated, Applicant has amended the specification to address the objections set forth on page 1, paragraphs 1-3 of the Office Action.

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The claims have been objected to on several grounds including improper multiple dependent language, and indefiniteness in the use of some claim language. Applicants submit that the new set of claims 34-62 address each of these objections. It will be noted that claim 19 was objected to on the ground that abbreviations should 15 be replaced by the full spelling of all of the coloring agents referred to therein (see new claim 52). This ground of objection is hereby traversed because the abbreviations set forth in claim 52 are well known and would be understood by those of ordinary skill in the art.

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Original claims 1 and 2 were rejected because of indefiniteness with respect to the type of gelatin employed in the composition. The claims have now been limited to fish gelatin for purposes of the present application thereby obviating the rejection of claims 1-2 under 35 U.S.C. Section 112. Applicants reserve the right to 5 pursue other types of gelatin disclosed in the present application in a continuation application.

Claim 32 stands rejected as being an improper use claim. This claim has been canceled and replaced by new claims 54-61 directed to a container for housing 10 a unit dosage form of an active agent employing the gelatin composition of claim 34.

Claims 1-3 stand rejected as anticipated by Soper (U.S. Patent No. 5,603,952). Soper is directed to a method of forming microencapsulated food or flavor capsules prepared by forming a mixture of a warm water fish gelatin and the 15 food or flavor particles in an aqueous medium and microencapsulating the particles by complex coacervation with at least two different colloidal materials to form microencapsulated capsules.

As is well known to a person skilled in the art, coacervation clearly differs from 20 a method of manufacturing gelatin compositions as in the present application through the typical use of a dip molding process. Coacervation provides under certain conditions a homogenous gelatin solution which can separate into two distinct liquid phases, a fairly concentrated gelatin solution and a very weak gelatin solution. The concentrated solution is referred to as the coacervate. Coacervation is

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used for systems containing gelatin together with a negatively charged macromolecule by adjustment of the pH to form microcapsules. This system is dependent upon there being a net positive charge on the gelatin molecules which is neutralized by the relative opposite charge of the other polymer. The microcapsules formed by coacervation must be cross-linked so as to form stable entities which can be removed from the aqueous solution.

5 Prior to the present invention, it was common knowledge in the art that gelatin derived from fish collagen lacked much of the gelling and setting ability of 10 mammalian gelatins. This results in the application of fish gelatins being fairly limited as described at page 2, lines 1-5 of the present application and as also set forth in the enclosed copy of a portion of an article entitled, "The Science and Technology of 15 Gelatin" wherein it is stated that fish gelatin lacks much of the gelling ability of mammalian gelatins due to a lower content of the amino acids proline and hydroxyproline.

Based on this knowledge, a person skilled in the art was of the opinion that although fish gelatin can be used for microencapsulation by coacervation, fish gelatin can not be used in a dip molding process under typical capsule-forming conditions 20 because it did not possess the gelling and setting ability typically associated with mammalian gelatins.

Applicants have developed a fish gelatin composition that can be routinely employed in a dip molding process for forming contains (e.g. capsules) through the

use of a hydrocolloid setting system which is not taught or suggested in the prior art. Because water solutions and fish gelatin remain liquid down to 10°C and water solutions of mammalian gelatin must be heated to over 30°C to remain liquid, one of ordinary skill in the art would view the behavior of fish gelatin as insufficient to be employed in a conventional dip molding process at conventional temperatures because of its significantly low gelling temperature. Accordingly, the disclosure in Soper of microencapsulation through coacervation does not lead one of ordinary skill in the art to a fish gelatin composition claimed herein uniquely suited for use in a conventional dip molding process.

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Claims 1-33 stand rejected over the combination of Soper, Chen (U.S. Patent No. 5,683,717), Wolff et al. (U.S. Patent No. 4,876,105) and Yamamoto et al. (U.S. Patent No. 5,756,123). Wolff et al. is stated to disclose gelatin compositions for food comprising a blend of gelatin, gellan gum and cations such as potassium, calcium magnesium or sodium. Chen is stated to teach gelatin coatings for medicines comprising gelatin, lecithin, a plasticizer and colorants. Yamamoto et al. is stated to teach capsule coatings comprising the combination of carrageenan, cations and gelling agents. The Office Action concludes that the combination of these references would lead one of ordinary skill in the art to the claimed invention.

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20 The rejection is hereby traversed and reconsideration is respectfully requested.

Wolff et al. discloses a dry blend consisting of gellan gum and gelatin which can contain mono-or divalent cations. As indicated at column 2, lines 13-15 gelatin is described as derived from collagen typically by boiling the skin, tendons, ligaments

and/or bones of animals in water. There is no teaching or suggestion in this reference of the use of fish gelatin, which unlike animal gelatin has distinct disadvantages because of its low gelling temperature. There is furthermore no teaching or suggestion in this reference of using gelatin compositions to make

5 containers (e.g. capsules) for housing active agents.

Chen describes a process for coating solid pharmaceutical medicaments.

There is no teaching or suggestion of formation of containers such as capsules for housing medicaments. Furthermore, Chen does not teach or suggest the

10 employment of a hydrocolloid setting system of the type claimed in the present application. As the Office Action recognizes, the examples of the Chen show the preparation of a gelatin solution containing animal gelatin, a plasticizer and a surface active agent in the absence of a hydrocolloid setting system.

15 Yamamoto et al. discloses a capsule shell which does not include gelatin at all but rather a gelatin substitute (hydroxypropylmethyl cellulose) and therefore is far afield from the present invention which employs fish gelatin and a system which overcomes the problems of using fish gelatin for forming containers such as capsules.

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In view of the foregoing, Applicants submit that the present application is in condition for allowance and early passage to issue is therefore deemed proper and is respectfully requested.

It is believed that no fee is due. However, if any fee is due, it should be charged to Deposit Account No. 23-0458.

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**TECHNOLOGY  
GRAPHS**

**E. M. MEAK  
J. E. SCOTT  
E. VON SYDOW**

**The Science and  
Technology of Gelatin**

**J. B. Koehler. PRINCIPLES OF  
FOOD, second edition. 1973.  
id edition. 1973.  
in INDUSTRY. Volume I - 1967.  
JUN. 1969.  
JUL. 1969.  
JUN. 1970.  
id edition. 1970.  
in FOOD PRODUCTS. Volume I -  
JUN. 1971.  
INTRODUCTION TO FOOD SCIENCE AND  
FOODSTUFFS. 1974.  
in 1. TECHNOLOGY PART A - 1974.  
in DRYING AND ADVANCED FOOD  
75.  
TECHNOLOGY OF GELATIN. 1977.**

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## INTRODUCTION

in the work of J. Pouradier and A. M. Venet (1952), J. D. Ferry (1948) established for low molecular weight gelatins ( $M_n$  45,000 and less) that gel "strength" (i.e. elasticity modulus of the gel under constant conditions) depended on molecular weight. Meanwhile the advance of protein chemistry, especially the refined techniques for amino acid analysis of A. C. Chibnall, allowed a reasonably accurate picture of the amino acid composition to be established.

It was clear to gelatin chemists concerned with the manufacture of gelatin that the process of gelatin making and the properties of the gels of gelatins of differing manufacture and source material were too complex to be explained by molecular weight changes alone.

The use of two distinct manufacturing processes provides a first point of difference. One involves extraction of the gelatin at a neutral or slightly acid pH, after cold alkaline pretreatment of the raw material. The second process, applied especially to pigskin, uses a brief soak in acid followed by extraction at a moderate temperature at about pH 4. The work of W. M. Ames (1953) in particular showed that the pretreatment with cold alkali hydrolysed ammonia from glutamine and asparagine residues leaving collagen with an isoionic point,  $pI$ , of 4.8 to 5.0. Acid pigskin gelatins retained glutamine and asparagine so giving a high  $pI$ , later shown to be as high as 9.0 to 9.3.

It had long been known that fish glue from fish skin and bones or even a fish gelatin made in the laboratory lacked much of the gelling ability of mammalian gelatins. In contrast, fish collagens of cartilaginous fish gave gelatins of better gelling power. These anomalies were shown by the amino acid determinations of J. E. Eastoe, A. A. Leach (1958) and others to relate to the contents of the amino acids, proline and hydroxyproline. A low content indicated poor gelling power.

The combination of the fractionation techniques and molecular weight determinations of G. Stainsby (1954) with gel rigidity studies by P. R. Saunders and A. G. Ward (1955, 1958) of these fractions and of materials degraded by heat or enzymes showed conclusively that gel rigidity for gelatins of molecular weight more than c. 50,000 hardly depended at all on molecular weight, but was determined by some unknown structural feature, which was reduced in its gelling effect by neutral or alkaline thermal degradation. A. Courts (1959) also showed that, if the gelatins had multichain molecules, the gelling power did not depend on the average chain length. This problem of the identity of the structural feature controlling gel strength has still, despite extensive further structural information (see A. Veis, 1964), not been fully resolved. An indication that it may arise from the scission of the polypeptide chains at the specific points of the sequence most involved in the initiation of gel formation has been put forward by G. Stainsby and R. J. A. Grand (1973). So there are still practical and theoretical problems

to be resolved  
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the physical stu  
may greatly aic  
the problem.

Side by side of gelatin has conversion of c mature mammal convertible to 1 in skin, bone a whose frequen temperatures w process is slow in progressive 1 pigskin has few with little pretr

In making gel in the raw material of suitable size, untouched the hydrogen bond into solution. N of a high proportion sufficiently high the Deutsche C sodium sulphate in the form of skins some 15-30 mm swelled extensively in crosslinking obtained by was reproducible in

A. G. Ward sodium sulphat 12-27°C. The collagen swelled optimal pretreat obtained. This is to industrial pre- pretreat collagen to be obtained. In these soluble

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